

REMARKS/ARGUMENTS

With this amendment, claims 37-48 are pending. For convenience, the Examiner's rejections are addressed in the order presented in a May 26, 2004, Office Action.

I. Rejections under 35 U.S.C. §103(a)

Claims 37-48 are rejected under 35 U.S.C. §103(a) as being allegedly obvious in view of Bulow *et al.*, *TIBtech* 9:226-231 (1991); Defrees *et al.*, WO 96/32491; and the common knowledge of the art of molecular biology provided by Sambrook *et al.*, pages 7.37-7.52 (1989) in further view of Gilbert(a) *et al. Eur. J. Biochem.*, 249:187-194 (1997) and Gilbert(b) *et al. Biotech. Lett.* 19:417-420 (1997). To the extent that the rejection applies to the amended claims, Applicants respectfully traverse.

To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference must teach or suggest all the claims limitations. MPEP§2143. See also *In re Rouffet*, 47 USPQ2d 1453. The court in *Rouffet* stated that "even when the level of skill in the art is high, the Board must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination." *Rouffet* at 1459. The court has also stated that actual evidence of a suggestion, or teaching, or motivation to combine is required and the showing of a suggestion, or teaching, or motivation to combine must be "clear and particular." *In re Dembiczak*, 50 USPQ2d 1614, 1617 (1999).

Applicants continue to assert that the cited references, alone or in combination, fail to teach or suggest all the elements of the claimed invention and fail to teach or suggest their combination to arrive at the claimed invention. Thus, Applicants continue to assert that a *prima facie* case of obviousness has not been provided in any of this or any previous Office Action.

Moreover, the claimed fusion proteins exhibit surprising properties that are not taught or suggested in any of the cited references. First, as indicated by the specification at page

45, lines 14-19, the claimed CMP-Neu5Ac synthetase- α -2,3-sialyltransferase fusion proteins are more soluble than an unfused α -2,3-sialyltransferase polypeptide. The claimed CMP-Neu5Ac synthetase- α -2,3-sialyltransferase fusion proteins are also more stable than the unfused α -2,3-sialyltransferase protein. In addition, the CMP-Neu5Ac synthetase- α -2,3-sialyltransferase fusion proteins are more efficient in a coupled reaction than are the unfused proteins.

The MPEP clearly states that evidence of unexpected results can be used to support a finding of nonobviousness of the claims. MPEP 716.01. Unexpected results that support a finding of nonobviousness include, *e.g.*, superiority of a property shared with the prior art or the presence of an unexpected property. MPEP 716.02.

The above listed advantages of the claimed fusion proteins are not shared with the teachings of the cited references. Bulow *et al.* teach that advantages of fusion proteins include only modest changes in K_m , pH-optima, thermostability, and stability to urea denaturation. However, Bulow *et al.* does not teach or suggest that a CMP-Neu5Ac synthetase- α -2,3-sialyltransferase fusion protein would also have increased solubility, or increased stability on storage, or increased efficiency for sialylation of lactose-FCHASE as compared to the unfused CMP-Neu5Ac synthetase and α -2,3-sialyltransferase proteins discussed in the other cited references.

Evidence of increased solubility of the claimed fusion protein as compared to the unfused α -2,3-sialyltransferase protein is found, *e.g.*, at page 45, lines 14-19, which state that the unfused α -2,3-sialyltransferase protein is not soluble at concentrations above 1 mg/ml in detergent, while the CMP-Neu5Ac synthetase- α -2,3-sialyltransferase fusion proteins are soluble to about 5 mg/ml in detergent. Thus, the claimed proteins have an unexpected property that is not found in the cited art. The specification also indicates that the CMP-Neu5Ac synthetase and α -2,3-sialyltransferase proteins are more stable than the unfused α -2,3-sialyltransferase proteins on storage at 4°C. See, *e.g.* page 39, lines 9-11 and page 45, lines 4-6.

Finally, Gilbert(b) *et al.* discloses that a coupled reaction using unfused CMP-Neu5Ac synthetase and α -2,3-sialyltransferase proteins converts 75% FCHASE-lactose to a sialylated form after sixty minutes. See, *e.g.*, Gilbert(b) *et al.* at page 420, left column. In

contrast, the specification discloses that the CMP-Neu5Ac synthetase- α -2,3-sialyltransferase fusion protein converts greater than 97% FCHASE-lactose to a sialylated form after sixty minutes. *See, e.g.*, specification at page 46, Table 1. Thus, the claimed fusion proteins show a surprising improvement over the art with regard to this characteristic.

As argued above, none of the cited references, alone or in combination, teach all the elements of the claimed invention. Nor do they provide a motivation or suggestion for the combination of references to arrive at the claimed invention. Moreover, as described above the claimed invention provides surprising advantages over the cited references, and thus, the rejection for alleged obviousness is inappropriate. In view of the above amendments and remarks, Applicants respectfully request that the rejections under 35 U.S.C. §103(a) be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,


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